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The Study on the Management after the Major Hepatectomy

by

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I. INTRODUCTION

Since WENDEL first succeeded in right hepatic lobectomy in 1910, many reports have appeared on major hepatectomy. Mean while, the use of antibiotics and the progress in blood transfusions and anesthesia, especially hypothermia, have increased the amount of liver which can be removed. Thus, major hepatectomy has reached the stage of being clinically feasible, at least in regard to the technical aspects.

However, the clinical prognosis is often poor and the mortality rate after major hepatectomy is still high. Of course, some patients die of recurrence of the malignant tumor, but those who die soon after operation have usually succumbed to functional failure of the residual liver.

Even though the residual liver is healthy before operation, it fails to function normally for some time after operation, and a residual liver with some pathological condition such as cirrhosis, will of course show more marked functional failure.

In either case, after major hepatectomy, the degree of recovery of function and of regeneration of the residual liver strongly influences the prognosis. Even though the liver has a good ability to regenerate and to compensate, all possible external aid should be given to facilitate progress from the degenerative to the regenerative period after operation.

Therefore, major hepatectomy was done experimentally in rabbits and infusion of several solutions were tested postoperatively mainly from the standpoint of carbohydrate metabolism. The residual liver was found to regenerate best when infusions of fructose solution were given following major hepatectomy.

II. EXPERIMENTAL MATERIALS AND EXPERIMENTAL METHODS

Healthy rabbits weighing 1.6~2.3 kg were used as experimental animals, since in this animal major hepatectomy can be performed easily without much stress because of the favourable anatomic conditions, and frequent blood-drawing and i. v. infusions can be done easily via the auricular veins. Moreover, rabbits are large enough so that the blood volume required for biochemical examinations can be withdrawn without adverse efforts.

The rabbit liver is mainly made up of 4 lobes : left anterior, left posterior, right anterior and right posterior. Their sizes are : left posterior lobe > left anterior lobe > right anterior lobe > right posterior lobe. The left posterior lobe, left anterior lobe and right anterior lobe cover up the stomach from above forward. This morphology and location of the liver are favourable for the operation.

Because the object of the present study was to compare the course after major hepatectomy, all operations were performed under the same conditions. Operations were performed in spring and autumn in order to avoid extremes of temperature. The diet consisted of about 200 g of vegetables and about 150 g of bean-curd refuse per day for 3 days and was stopped about 10 hours before the operation.

The anesthesia was light enough so that the animals moved their legs slightly during the operation. For anesthesia, intraperitoneal or intravenous pentobarbital sodium solution was tried first, but the animals never awakened and died 3~4 hours after the operation without any gross evidence at autopsy of complications such as postoperative bleeding. The cause of death was apparently accumulation of pentobarbital, which is usually hydrolysed mainly in the liver: major hepatectomy presumably slows hydrolysis by reducing the volume of the liver. Next, ether by insufflation was tried, but although the animals awakened from the anesthesia, their condition deteriorated, and they died 3~4 hours after the operation. Thus, ether also appears to be contraindicated when there is extreme dysfunction of the liver.

Finally, fluothane anesthesia was used, since this is believed to cause smooth introduction and awakening and minimal liver damage. The animals awakened smoothly from the anesthesia and none of them died within 4 hours after the operation. Therefore, fluothane was used in these experiments.

The Method of Operation

The operative field was disinfected and penicillin (150,000 units) was injected intramuscularly. Then a median incision was made in the epigastrium, and mattress-sutures were placed at the hilus of the left anterior lobe and the right anterior lobe and the central portion of the left posterior lobe. Then lobectomy was performed, and the cut surface of the liver was covered with great omentum in order to prevent intestinal adhesions. The incision was always closed by sutures in two layers.

In order to compare the postoperative courses, one must always resect the same amount of liver. Many studies performed to determine the limits of resectability of the liver have shown that in healthy experimental animals 65~85 % hepatectomy is the upper limit. However, soon after the operation, slight dysfunction of the residual liver has been noted even after only 20 % hepatectomy, and marked dysfunction after 50 % hepatectomy. In the present study, 60~70 % hepatectomy was used.

In calculating the percentage of hepatectomy, the author estimated roughly the weight of the whole liver from the body-weight of the animal by means of the formula introduced by YAMADA:

$$Y = 30.2 (X - 24.5) + 73.4$$

Y: weight of whole liver (g)

X: body-weight (kg)

(in rabbits weighing 1.5~3.4 kg)

During operation the ratio of resected liver to the weight of the whole liver was determined, and if this was too low, more liver was resected. Thus the percentage of hepatectomy was fairly uniform.

After the operation, some rabbits were used as controls and received no infusion at:

all, and the others were divided into 6 groups: 1) infused with 10 % crystal amino acid solution, 2) infused with 50 % glucose solution, 3) infused with 50 % glucose solution + insulin, 4) infused with 20 % glucose solution + insulin, 5) infused with 5 % glucose solution and 6) infused with 5 % fructose solution.

The infusion of each solution was begun 2~5 hours after the operation and repeated every 12 hours until the animals died or began to eat spontaneously. Vit. B complex and Vit. C were given with each infusion and the volume of each infusion was 10 cc per kg of body-weight. The solution was infused as slowly as possible (15 minutes per 20 cc of solution) via an ear vein. The insulin dose was 0.1 units per kg of body-weight and it was injected intramuscularly immediately before the infusion of the glucose solution.

The rate of survival in each group, blood biochemistry, rate of regeneration of the residual liver and its glycogen and protein content and histological findings were determined.

Animals in which autopsy revealed postoperative bleeding, ileus, peritonitis etc. were excluded from the calculation of the survival rate.

Blood glucose was measured by FOLIN-WU's method, serum albumin by YOSHIKAWA-SAITO's method and liver function by Brom-Sulphalein (B. S. P.) retention and thymol-turbidity test (T. T. T.).

The rate of regeneration of the residual liver was calculated by the method proposed by ISHIGURO,

$$\text{rate of regeneration} = \frac{C - (A - B)}{A} \times 100 \%$$

A: weight of whole liver before operation

B: amount of excised liver

C: amount of residual liver

(When the rate of regeneration equals the rate of hepatectomy, the residual liver has been restored to its preoperative weight.)

The glycogen content of the residual liver was determined by heating a fresh slice of liver and hydrolysing it with H_2SO_4 -solution (glycogen \rightarrow glucose); then this glucose was measured by FOLIN-WU's method. 0.927 times the amount of this glucose equals the amount of glycogen in that slice of liver.

The protein content of the residual liver was measured by KJELDAHL's method.

In the histological examination of the residual liver, hematoxylin-eosin, Sudan III and PAS stains were used.

III. EXPERIMENTAL RESULTS

(1) Survival rate

Only one of the 12 controls lived for more than a month, but then gradually became emaciated and died about 4 and a half months after the operation. Of the 17 rabbits infused with 5 % fructose solution 9 rabbits survived for more than a month; then one died of diarrhea 40 days after the operation and another died of ileus due to adhesion 3 months after the operation. The other 7 rabbits all had good appetites and were healthy until they were sacrificed 6 months after the operation. Since the rabbits that survived for more than a month were already free of the direct influence of major hepatectomy, it seems feasible to compare of survival rates one month after the hepatectomy.

Table 1. Survival rate in each group

group	survival rate	
	over 11 days	over one month
Control	8.3%	8.3%
10% amino acid group	0	0
50% glucose group	0	0
50% glucose + insulin group	0	0
20% glucose + insulin group	0	0
5% glucose group	33.3	26.7
5% fructose group	70.6	52.9

Table 2. Course soon after operation

group	total number of rabbits	number surviving in each period					
		24 hours	24~48 hours	48~72 hours	4~10 days	11~29 days	over one month
Control	12	6	2	3	0	0	1
5% glucose group	15	3	2	3	2	1	4
5% fructose group	17	1	3	1	0	3	9
Other groups	17	9	7	1	0	0	0

As is shown in Table 1, the survival rate was highest in the group infused with 5 % fructose solution, in which the majority survived for more than a month, followed by the group infused with 5 % glucose solution. All rabbits in the other groups died within 72 hours after the operation.

Infusions were given every 12 hours and rabbits dying within 72 hours after the operation never ate spontaneously, but those which survived longer than 72 hours began to eat a little on about the third day and ate a regular diet on the 4th or 5th day, at which time the infusions were discontinued. In these rabbits, the total volume of infused solution was 70~80 cc per kg of body-weight.

(2) Results of biochemical examination of blood.

In healthy rabbits, the blood glucose level is 110~120 mg/dl (BANG) and the serum albumin level is 5.51 g/dl (DUKES).

Table 3. Blood glucose and serum albumin levels of controls after the operation (average)

	time after the operation			
	20 hours	30 hours	50 hours	80 hours
blood glucose	47 mg/dl	49 mg/dl	47 mg/dl	40 mg/dl
serum albumin	3.14 g/dl	3.29 g/dl	3.25 g/dl	3.30 g/dl

The controls showed marked hypoglycemia and hypoalbuminemia soon after the operation (Table 3).

On the contrary, in the rabbits infused with 5 % glucose or fructose solution, as is shown in Tables 4 and 5, the blood glucose levels returned promptly to normal, more

Table 4. Blood glucose and serum albumin levels of group infused with 5% glucose solution (average)

interval	3 days	7 days	14 days	21 days	28 days	60 days
blood glucose	92 mg/dl	131 mg/dl	103 mg/dl	—	—	—
serum albumin	2.78 g/dl	3.24 g/dl	3.20 g/dl	3.36 g/dl	3.27 g/dl	4.88 g/dl

Table 5. Blood glucose and serum albumin levels of group infused with 5% fructose solution (average)

interval	3 days	7 days	14 days	21 days	28 days	60 days
blood glucose	116 mg/dl	159 mg/dl	102 mg/dl	—	—	—
serum albumin	3.23 g/dl	3.17 g/dl	3.18 g/dl	3.47 g/dl	3.12 g/dl	4.35 g/dl

rapidly in those receiving 5 % fructose solution. The results of liver function test were also better in the group infused with 5 % fructose solution. But in both groups serum albumin levels returned to normal very slowly, indicating, as many workers have stated recently, that protein must be supplied at the same time.

Table 6. Liver function soon after operation (second day) in group infused with 5 % glucose or fructose solution (average)

group	test	B. S. P. test	T. T. T
5 % glucose group		12.5%	2 units
5 % fructose group		0	2 units

For the B. S. P. test, Hepatosulphalein solution was injected in a dose of 5 mg per kg of body-weight into a vein of the ear and after 45 minutes blood was drawn from a vein of the other ear.

(3) Regeneration of the residual liver in rabbits infused with 5 % glucose or fructose solution.

Table 7. Rate of regeneration of the residual liver in group infused with 5% glucose solution (average)

days after operation	2	3	15	over 90
rate of regeneration	8.3%	23.5%	49.4%	81.3%

Table 8. Rate of regeneration of the residual liver in group infused with 5% fructose solution (average)

days after operation	2	3	22	28	over 90
rate of regeneration	19.5%	43.8%	52.9%	60.4%	72.1%

The rate of regeneration of the residual liver soon after operation, as is shown in Tables 7 and 8, was higher in the 5 % fructose than in the 5 % glucose infused group, but 15~22 days after the operation there was no significant difference between the two groups.

Thus, the infusion of 5 % fructose solution affects regeneration most favorably soon after operation when the function of the liver is most disturbed and the mortality rate is the highest.

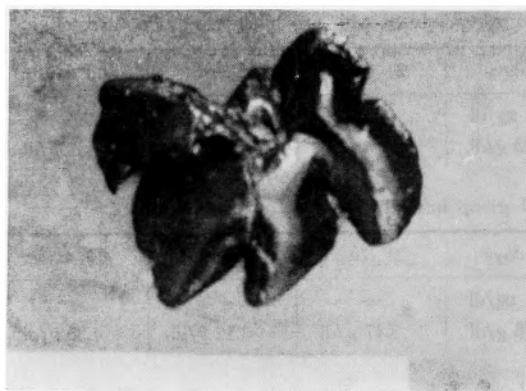


Fig. 1 Normal liver of rabbits

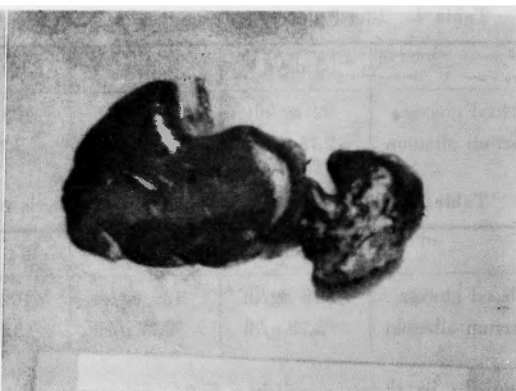


Fig. 2 60% excised liver; 143th day after operation, rate of regeneration 68.3%

As illustrated in Figs. 1 and 2, regeneration of the residual liver progressed best in the right posterior lobe, which had not been excised at all, whereas the lobes which had been excised partially (for instance, the left posterior lobe) showed almost no change in size.

- (4) Glycogen content of the residual liver in rabbits infused with 5 % glucose or fructose solution.

Table 9. Glycogen content of the residual liver (per g) in group infused with 5% glucose or fructose solution (average)

days after operation	2	3	15	22	28	over 90
5% glucose group	8.0mg	7.4mg	40.0mg	—	—	121.9mg
5% fructose group	21.0mg	23.5mg	—	115.2mg	101.0mg	94.5mg

The glycogen content of the liver in healthy rabbits averages 84.9 mg per g of liver.

As is shown in Table 9, after major hepatectomy the glycogen content of the residual liver decreased markedly, but soon after the operation the group infused with 5 % fructose solution maintained a much higher liver glycogen content than the group infused with 5% glucose solution.

- (5) Protein content of the residual liver in rabbits infused with 5 % glucose or fructose solution.

Table 10. Protein content of the residual liver (per g) in group infused with 5 % glucose or fructose solution (average)

days after operation	2	3	15	22	28	over 90
5% glucose group	191.0mg	190.6mg	192.6mg	—	—	182.6mg
5% fructose group	197.6mg	196.5mg	—	199.9mg	184.9mg	194.1mg

The protein content of the liver in healthy rabbits averages 191.4 mg per g of liver.

As is shown in Table 10, the protein content of the residual liver remained normal in both groups.

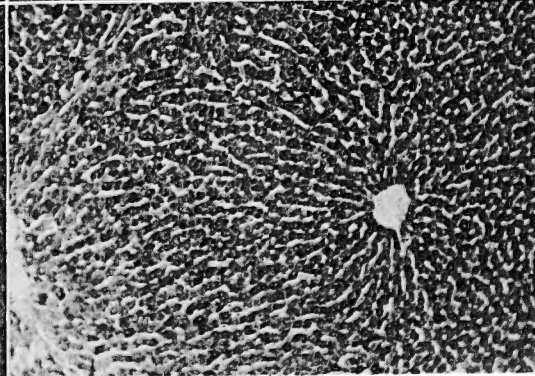
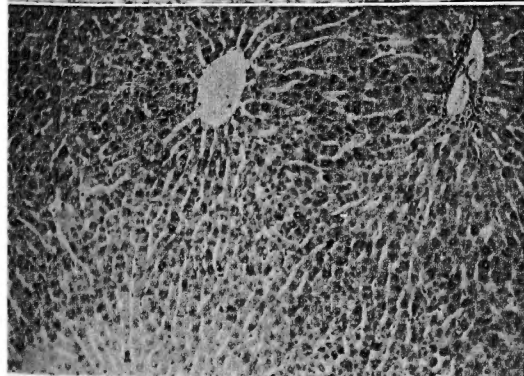
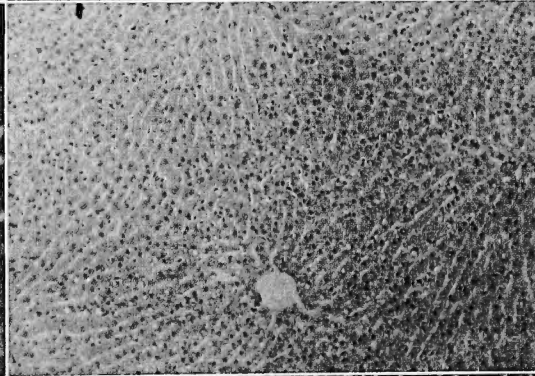
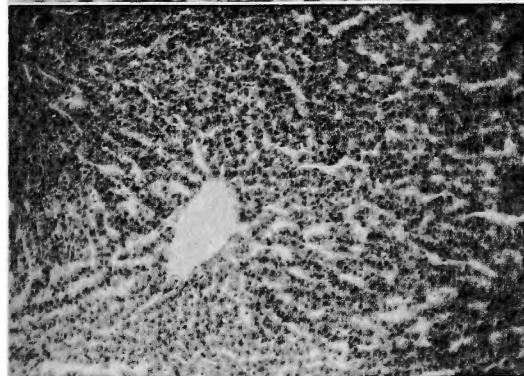
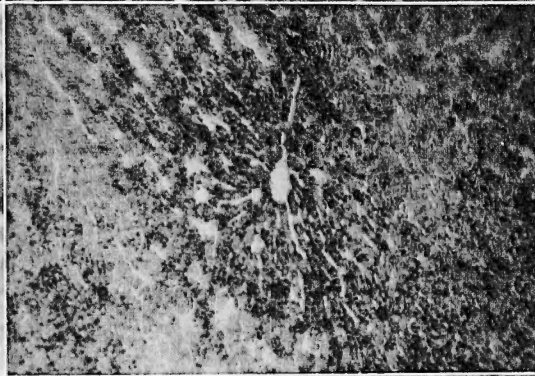
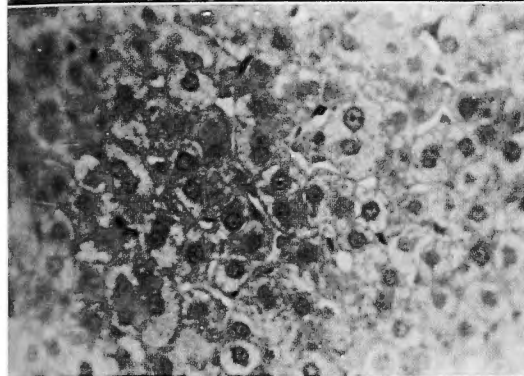
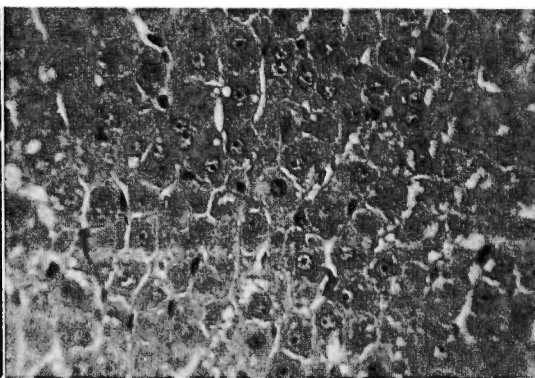
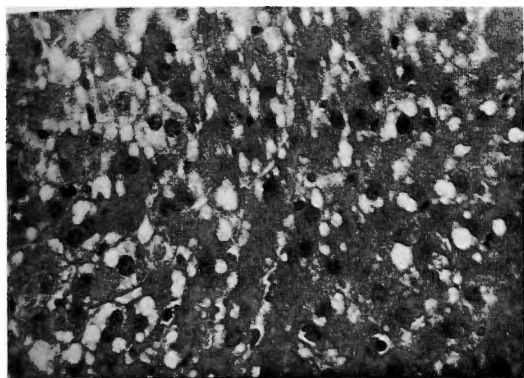


Figure 3

H. E. stain, 5% glucose group, second day after operation × 400

Figure 4

H. E. stain, 5% fructose group, second day after operation × 400

Figure 5

H. E. stain, 5% fructose group, 22th day after operation $\times 400$

Figure 6

Sudan III stain, 5% glucose group, third day after operation $\times 100$

Figure 7

Sudan III stain, 5% fructose group, third day after operation $\times 100$

Figure 8

PAS stain, 5% glucose group, third day
after operation $\times 100$

Figure 9

PAS stain, 5% fructose group, third day after operation $\times 100$

Figure 10

PAS stain, 5% fructose group, 28th day after operation $\times 100$

- (6) Histological findings in the residual liver in the groups infused with 5 % glucose or fructose solution.

i) Hematoxylin-eosin stain

Table 11. Hematoxylin-eosin stained specimens of the residual liver in group infused with 5 % glucose solution

days after operation	2	3	4	15
degree of vacuolar degeneration	##	##	+	—
degree of collapse of nuclei	++	++	+	+
irregularity of cell columns	++	##	++~+	++~+
degree of mitosis	±	±	+	+

Table 12. Hematoxylin-eosin stained specimens of the residual liver in group infused with 5 % fructose solution

days after operation	2	3	22	28
degree of vacuolar degeneration	+	±	—	—
degree of collapse of nuclei	+	+	±	±
irregularity of cell columns	+	+	±	—
degree of mitosis	±	+	++	+

As is shown in Tables 11 and 12, signs of degeneration were seen in both groups after the operation; large and small vacuoles in the cytoplasm and collapsed or obscure nuclei. The liver cell columns were irregular and partly collapsed. Of course, these signs of degeneration were severe soon after the operation and gradually decreased. Next, mitosis became evident and signs of regeneration were conspicuous. The 5 % fructose group showed less severe signs of degeneration and smoother and more rapid regeneration than the 5 % glucose group (Figs. 3, 4 and 5).

ii) Sudan III stain

Table 13. Sudan III stain of the residual liver in group infused with 5 % glucose solution

	days after operation	2	3	4	15
fat droplets	quantity	##	###	+	+(※)
	location	central~intermediate zone of acinus	central ~ peripheral zone of acinus	diffuse	peripheral zone of acinus ~ GLISSON's capsule
	size	mostly small	mostly small	small	large

Table 14. Sudan III stain of the residual liver in group infused with 5 % fructose solution

	days after operation	2	3	22	28
fat droplets	quantity	+	+	±(※)	±(※)
	location	central~intermediate zone of acinus	mainly intermediate zone of acinus	peripheral zone of acinus~GLISSON's capsule	peripheral zone of acinus~GLISSON's capsule
	size	small	mostly small	small	mostly small

As is shown in Tables 13 and 14, fatty degeneration was noted, with fat droplets present up to the central zone of the liver acinus. Degeneration was marked in the 5 % glucose group, especially on the second and third days after the operation, but was very mild in the 5 % fructose group (Figs. 6 and 7).

In the cases marked (✱✱) in Tables 13 and 14, the fat droplets seen in the periphery of liver acini or GLISSON's capsule appear to be physiological and not due to degeneration.

iii) PAS stain

Table 15. PAS stain of the residual liver in group infused with 5 % glucose solution

glycogen	days after operation	2	3	4	15
	quantity	+	±	+	###
	location	mainly central zone of acinus	slightly central zone of acinus	central zone of acinus	almost completely diffuse

Table 16. PAS stain of the residual liver in group infused with 5 % fructose solution

glycogen	days after operation	2	3	22	28
	quantity	##	††	#### (full)	#### (full)
	location	central~intermediate zone of acinus	mostly diffuse	diffuse	diffuse

As is shown in Tables 15 and 16, after major hepatectomy in the 5 % glucose group, there was a marked decrease of glycogen in the residual liver but in the 5 % fructose group the amount of glycogen in the residual liver remained fairly high even on the second or third days after the operation. In both groups the glycogen content of the residual liver had returned to normal by the 22th day after the operation (Figs. 8, 9 and 10).

IV. SUMMARY AND DISCUSSION

In 1918 SUENAGA reported the changes occurring in rabbits after experimental hepatectomy, and in 1929 FISCHERFACH and others reported that after 70 % hepatectomy the residual liver of rats returned to its preoperative weight within about 2 weeks and that of dogs within about 5 weeks; this demonstration that even if a fairly amount of liver is excised, the residual liver can regenerate rapidly, has been generally accepted.

However, SHIMURA and others have shown that the prognosis after major hepatectomy depends on the degree of restoration of function of the residual liver and of the regeneration of the residual liver (Of course, operative technique and complications are also important.).

According to SHIMURA, LIN, MC DERMOTT and others, there is temporary dysfunction of the residual liver after major hepatectomy, as evidenced by elevation of serum bilirubin, C. C. F., T. T. T., B. S. P. retention and alkaline phosphatase activity, along with a marked lowering of the serum protein, especially serum albumin, and blood glucose levels. Moreover, HONJO, MIKAMI, OKUMURA and DRAPANAS reported a marked elevation of B. S. P. retention, and lowering of blood glucose and serum protein levels soon after

major hepatectomy in rabbits or dogs. The B. S. P. and serum protein level returned to normal in about 4 weeks and the blood glucose level in 1 to 2 weeks after operation. The histological findings in the residual livers after major hepatectomy were those of degeneration, such as irregularity or rupture of the cell columns, vacuolar degeneration, collapse of the nuclei, fatty degeneration and marked decrease of glycogen. These were followed by signs of gradual recovery, then proliferation and finally a normal appearance.

If this dysfunction and degeneration in the residual liver after operation can be reduced and regeneration can be stimulated, a better prognosis can be achieved.

Previous reports on nutritional management after major hepatectomy have emphasized the necessity of improving protein metabolism and have tended to neglect carbohydrate metabolism.

Therefore, the present study deals mainly with carbohydrate metabolism in an effort to lower the great mortality after major hepatectomy.

After major hepatectomy, the control animals, which received no infusions at all after the operation, had a one month survival rate of only 8.3 %, and severe hypoglycemia and hypoalbuminemia were noted soon after the operation. It appeared that although glycolysis in the liver was greatly accelerated by the operation, the insufficient nutritional supply after the operation resulted in severe hypoglycemia.

Moreover, since albumin is synthesized only in the liver, the severe hepatic dysfunction and decrease of liver volume after major hepatectomy cause, on the one hand, a marked decrease in the ability to synthesize albumin and, on the other hand, a rapid breakdown of protein by the operative stress, which are reflected in the severe hypoalbuminemia noted after major hepatectomy.

Of course, since the controls received no infusions at all, extreme dehydration was also present, which hastened death in the controls.

As mentioned already, after major hepatectomy, even if carbohydrate and water are supplied by infusions of 5 % fructose or 5 % glucose solution, severe hypoalbuminemia is still present. So, protein must also be supplied.

However, in the group infused with 10 % crystal amino acid solution, the survival rate was not improved at all. Many studies have been made on the infusion of amino acid solution. BROUNE and others are of the opinion that in the catabolic phase the infusion of amino acid solution is seldom effective and may indeed damage the kidney; on the other hand, there have been a few reports that the infusion of amino acid solution greatly shortens the catabolic phase. In either case, because the ability to synthesize albumin from amino acids is low when there is marked dysfunction of the liver, and because of the great decrease in the volume of the liver, as mentioned by FLOCK and OBARA, the infusion of amino acid solution is not helpful after major hepatectomy.

Therefore, it seems more rational to supply protein directly as serum albumin or plasmanate composed mainly of albumin. Though supplementation of protein is important for the regeneration of the liver as mentioned by DAVIS, GURD and DENTON and for the restoration of body-weight after surgery as described by KINOSHITA, it would seem to be more effective during the anabolic phase and even when given in the form of protein soon after operation, it may not lower the mortality rate. Therefore, the present study concentrated on the significance of carbohydrate supplementation soon after major hepatectomy.

ectomy.

As was noted in the controls, severe hypoglycemia occurred right after major hepatectomy. Therefore, infusion of 50 % glucose solution was first attempted, with the thought that it might be better to supply enough calories at the same time. But, this did not improve the survival rate at all, perhaps because the decrease in total volume of the liver and the dysfunction of the liver resulted in excessive hyperglycemia. Therefore, insulin was injected intramuscularly along with infusion of 50 % glucose solution, but still there was no increasing the survival rate.

Insulin plus the infusion of 20 % glucose solution was also ineffective in reducing the mortality rate after major hepatectomy.

In the next group, isotonic 5 % glucose solution was infused. The survival rate increased and the survivors began to eat spontaneously about 3 days after the operation. The blood glucose level in these survivors was already almost normal (92 mg/dl) on the third day after the operation and the one month survival rate was 26.7 %.

Recently the differences between fructose and glucose metabolism have attracted attention and it is said that fructose is more effective than glucose in stimulating the production of pyruvic acid in the liver and therefore that it is metabolized more promptly and smoothly and with a greater production of energy which then leads to a greater production of glycogen. In fact, according to CORI, when fructose is given, 3 times as much glycogen may be produced in the liver as when the same volume of glucose is given. Moreover, EPPINGER and others demonstrated that fructose has a greater protein-sparing action than glucose, and LAMPRECHT and others showed that fructose can be metabolized without the influence of insulin. Recently it has been recognized that fructose has a stronger antidotal action in the liver than glucose. KOBAYASHI showed that the more the liver was damaged, the greater was the antidotal action of fructose. Therefore, the effect of infusions of 5 % fructose solution after major hepatectomy was next investigated.

The group infused with 5 % fructose solution had a much higher survival rate than the group infused with 5 % glucose solution, and the number of survivors living for a long period increased extremely. The blood glucose level was already normal on the third day after hepatectomy. The B. S. P. test was normal on the second day, about 33 hours, after the operation. IKUSHIMA reported that infusions of glucose promote the ability of the liver to excrete B. S. P., but this ability is promoted even more by infusions of fructose.

In the 5 % fructose group, regeneration of the residual liver proceeded about twice as fast as in the 5 % glucose group soon after the operation.

Histological examination of hematoxylin-eosin stained specimens showed less degeneration in the fructose group than in the glucose group and a more rapid transition to the regeneration period.

The glycogen content of the residual liver was larger soon after the operation in the fructose group than in the glucose group. This tendency was also noted in the PAS stained material, which showed that the production of glycogen began in the central zone of the liver acinus.

IKUSHIMA and OKAZAKI examined normal liver of rabbits and OKAZAKI also studied livers damaged with CCl_4 or P, and they demonstrated that the production of glycogen

is greater with fructose than with glucose administration. Fructose is still more effective than glucose when liver damage is severe. Therefore, it is especially necessary to give fructose when the liver is damaged; the present study confirmed this fact well.

Hematoxylin-eosin and Sudan III stains showed degeneration in both fructose and glucose groups, but in fructose group, degeneration was slight and the tendency to move promptly to the regenerative process was greater than in the glucose group. In the glucose group, fatty liver occurred soon after the operation but it was seldom seen in the fructose group. These findings show distinctly that fructose is utilized effectively even when the function of the liver is greatly decreased as after major hepatectomy and that glucose can be utilized much less readily.

In this connection, the results of experiments with C^{14} -labeled fatty acids are of interest. They show that when carbohydrate metabolism is disturbed, fat is not stored as depot fat at all but accumulates in parenchymal organs. Then, when carbohydrate metabolism improves, surplus fat moves rapidly into the normal depôts and only the required quantity of fat moves into parenchymal organs and is used there.

These experimental results show that after major hepatectomy infusion of fructose solution is very effective—much more so than that of glucose solution—in reducing mortality and morbidity soon after the operation which was a great cause of death after major hepatectomy in the past.

V. CONCLUSION

These experiments were designed to lower the mortality rate soon after major hepatectomy mainly by improving carbohydrate metabolism.

The results lead to the following conclusions:

- 1) In order to reduce the mortality soon after the operation which was a great cause of death after major hepatectomy, it is most important to infuse 5 % fructose solution and thus to improve carbohydrate metabolism and liver function.

- 2) When there is severe dysfunction of the liver as after major hepatectomy, carbohydrate metabolism and liver function can not be restored rapidly enough by the infusion of glucose solution.

- 3) Improvement of carbohydrate metabolism and liver function soon after the operation reduces the degeneration after major hepatectomy as much as possible and promotes prompt and smooth regeneration.

- 4) Since the fatty liver occurring soon after major hepatectomy is secondly to disturbed carbohydrate metabolism, the improvement of carbohydrate metabolism may prevent fatty liver.

- 5) After major hepatectomy, of course supplementation with protein is also indispensable, but immediately after operation the improvement of carbohydrate metabolism is of primary importance.

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和文抄録

肝広汎切除の術後対策に関する研究

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肝広汎切除直後の死亡率を軽減せしめるためには如何なる対策を講ずべきかを、主として糖代謝の面より検討した。即ち、実験的に家兎を用いて60~70%の肝広汎切除を行ない、術直後よりアミノ酸液、高張ブドウ糖液、5%ブドウ糖液及び5%果糖液等を夫々単独に輸注せる群を作製し、各群の生存率、血液生化学的性状、肝機能及び残存肝の組織像等について比較検討を行ない、次のような結論に達した。

1) 肝広汎切除時の大きな死亡の原因となつた術直後の死亡率を軽減せしめるためには、5%果糖液の輸注を行ない、糖代謝の改善を、ひいては肝機能の改善を図ることが最も大切である。

2) 肝広汎切除時のような著しい肝機能低下のある場合には、ブドウ糖液の輸注では、術直後の充分な糖代謝の改善、肝機能の改善は望み得ない。

3) 術直後の糖代謝の改善、肝機能の改善は、肝広汎切除後の退行性変性を可及的に軽減し、より速やか且つ円滑に再生機能を営ましめることになる。

4) 肝広汎切除直後の脂肪肝は、糖代謝の障礙に基づく二次的のものであり、従つて糖代謝の改善により、自ら之の発来は防止される。

5) 肝広汎切除に際しては、蛋白質の補給も亦必要、不可欠なことは、いうまでもないが、まず術直後には、糖代謝の改善が第一義的意義を有する。